REMARKS

Claims 1-41 are active in this application. Claims 1 and 12 have been amended for clarity. In addition, Applicants affirm the election of Group I, Claims 1-7. Consistent with the Examiner's comments on page 3 of the Official Action, Applicants request that upon finding the elected claims allowable, the corresponding non-elected process claims be rejoined (M.P.E.P. § 821.04).

The Examiner has asserted that the specification only describes one species of the claimed modified enzyme, particularly noting the sequence in SEQ ID NO: 2 and therefore contends that the claims are neither enabled nor adequately described. Applicants disagree and will point to specific portions of the specification and the knowledge in the art, which supports the present claims.

First, at the time of the present invention, alcohol dehydrogenase enzymes were well-known and the structures of these enzymes were also known (referring to the discussion on page 9 of the present specification). Even a cursory review of publicly available sequence data banks supports that were hundreds of alcohol dehydrogenase enzymes, whose sequences were known. In addition to the alcohol dehydrogenase enzymes, the Applicants have also described numerous other enzymes which can be modified in accordance with the present invention (see pages 9-10).

The present invention lies in the discovery that the replacement of neutral amino acids with acidic amino acids while leaving the basic amino acids unchanged, results in a more active enzyme molecule. Since the sequences are known, the locations of the coenzyme binding sites were known or readily identifiable, the acidic, basic, and neutral amino acids are known, methods of effecting amino acid substitution are known (and also described in the present specification, for example, page 6 through page 9), techniques for determining NAD(H) affinity are known, there is no question that the claims are, in fact, enabled.

Turning to the written description part of the rejection, the structures of the enzymes to be modified are, in fact, known (see the above discussion). The structures of neutral and acidic amino acids are also known. The structure of an enzyme which has had one or more of its' neutral amino acids in the coenzyme binding site changed to an acidic amino acid can readily be envisioned by the skilled artisan. Therefore, Applicants have described:

1. the distinguishing attributes the claimed enzyme possesses (increased NAD(H) affinity correlative to the replacement of neutral amino acids with acidic amino acids); and
2. the limit on what types of modified enzymes the claims cover as well as the specific changes to the known enzyme structures (only those enzymes that have increased NAD(H) affinity, no basic amino acids changed in the coenzyme binding site, and at least one neutral amino acid changed to an acidic amino acid in the coenzyme binding site);

In view of this detailed guidance and description coupled with the readily available information in the art, certainly the claims are adequately described within the meaning of 35 U.S.C. § 112, first paragraph.

Therefore, withdrawal of both grounds of rejection under 35 U.S.C. § 112, first paragraph is requested.

The present claims are not anticipated by the Hummel (U.S. Patent 6,413,750) disclosure because Hummel does not describe the claimed modified enzyme where at least one neutral amino acid of the wildtype enzyme is replaced with at least one acidic amino acid in the coenzyme binding site and where basic amino acids at the coenzyme binding site are not replaced.

In particular, Hummel describes in column 1, lines 66 through column 2, line 5 that reduction in basicity in the docking area of the enzyme through corresponding alterations in

amino acid sequence is necessary, i.e., Hummel describes to alter the basic amino acid sequences. This is also described in col. 2, lines 34-36 : "in the following Examples 1-4, **basic amino acids were replaced** by neutral amino acids at the location R38, H39, K45 and/or K48" (emphasis added). Therefore, the entire disclosure of Hummel is directed to the replacement of primarily basic amino acids in the coenzyme binding site. This is the complete opposite of what is claimed in the pending claims.

While in Example 5 of column 17 of Hummel describe the conversion of glycine 37 to aspartic acid (which corresponds to the aspartic acid at position 38 in SEQ ID NO. 2 of the present application), there is no question by reading the entire Example, what is actually described is a combination mutant where this particular G37D mutant accompanies three other mutations; i.e., alanine 9 to glycine, arginine 38 to leucine and lysine 48 to methinine. Notwithstanding what may be claimed in the Hummel patent, the entire patent is directed to the replacement of basic amino acids at the coenzyme binding site which again is not what is in the present claims. Therefore, the rejection under 35 U.S.C. § 102(e) is untenable and should be withdrawn.

The rejection of the claims under 35 U.S.C. § 112, second paragraph is addressed by amendment.

Applicants submit that the present application is now ready for allowance. Early notification of such allowance is kindly requested.

Respectfully submitted,

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